Medical and Research Publications
International Open Access

Review Article **Journal of MAR Oncology (Volume 3 Issue 6)**

Pharmacoeconomics with Special Emphasis in Oncology

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Received Date: April 04, 2022

Published Date: May 01, 2022

Abstract

Economic pressures on health care systems, the undeniable visibility of the amount of drug consumption and the growing competition for the market have contributed to the development of methods to assess health costs.

Cancer is one of the main current problems related to health and its consequences go beyond the strictly health field due to its social and economic impact.

Introduction

When the expenses represented in health are analyzed according to US statistics, a progressive growth in costs is observed from 1961 to 2023, according to the National Institute of Health, cancer represented in the US in the year 2000 a cost of 180 billion dollars, 60 in direct costs and 120 in indirect costs related to lost productivity and premature mortality. Hospitalization costs for cancer patients represent 75% of the overall cost of the disease, while the cost of chemotherapy can range between 6 and 15%. (See Fig. 1).

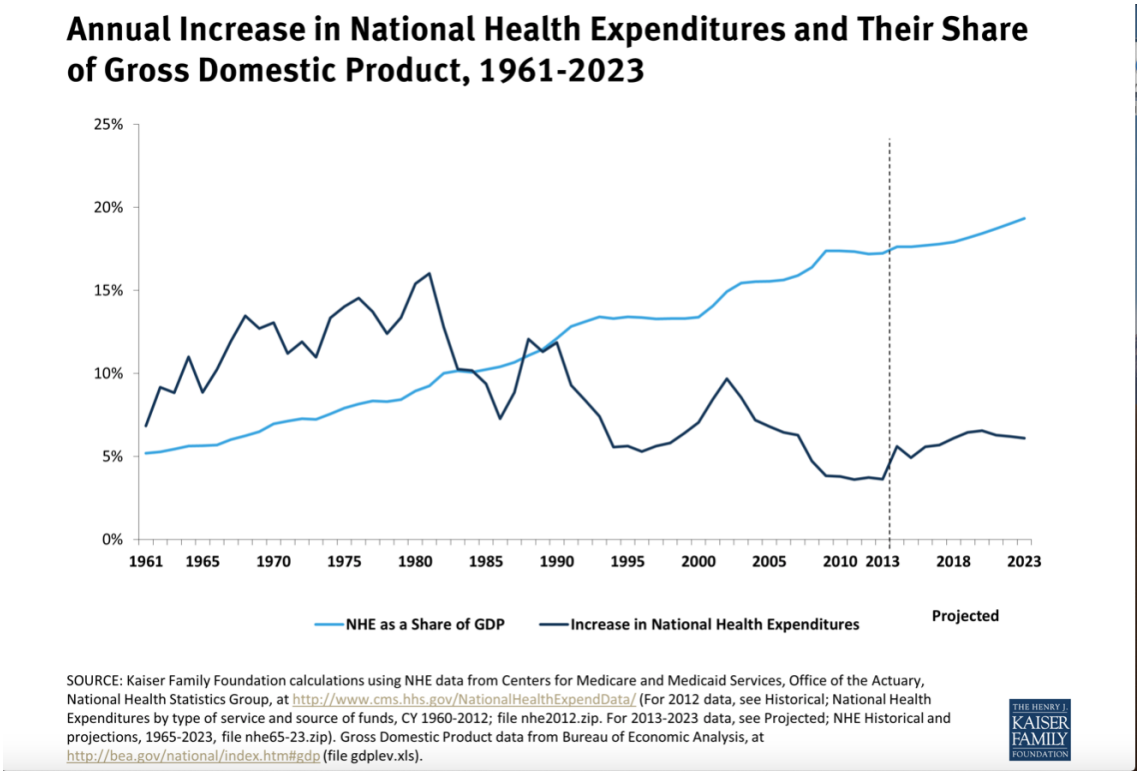

Fig. 1. Annual Increase in National Health Expenditures and their share of gross domestic product, 1961-2023

Medicines have an important economic impact for the health system, the economic evaluation of medicines identifies, analyzes, and compares the costs, benefits, and risks of pharmacological treatments. The increase in spending on medicines has been attributed to various causes, some known, such as demographic factors and specifically the aging of the population, one of the most important. Another factor that contributes to the increase in spending is a consequence of the technological advances that new drugs have brought about, usually with a higher acquisition cost than the available standard therapies. The cost of chemotherapy has increased notably in recent years because of the introduction of new high-cost cytotoxic agents, adding the added costs derived from support therapy (colony-stimulating factors, artificial nutrition, antiemetics).

It is important to note, however, that the cost of drug therapy is a generally minor component of the overall cost of disease. Hospitalization, rehabilitation, and indirect costs often have a higher cost, especially in chronic pathologies that affect patients of productive age.

What is Pharmacoeconomics?

It is the area of health economics focused on the analysis of pharmaceutical products. Pharmacoeconomics is the study of the costs and benefits of medical treatments and technologies, combining economics, epidemiology, decision analysis, and biostatistics. Analyzes the costs and consequences of medicines and their effects on individuals, health systems and society.

To study the efficiency of any pharmacological treatment, it is necessary to consider, on the one hand, the costs, defined as resources used with their corresponding monetary value, and, on the other hand, the consequences, defined as results achieved.

Consequences are understood as any result achieved with the use of resources, and three different types of consequences can be considered: effects, utilities, and benefits.

Effects are objective clinical consequences measured in physical or natural units, for example: lives saved, years of life gained, days of pain avoided, time free from illness, days of hospitalization avoided.

Utilities are subjective consequences that are measured in units of quality of life, and that fundamentally interest the subject or patient: the measure of quality of life related to health, and social values or preferences.

Benefits are material consequences that are measured in monetary units and that are of fundamental interest to the financier.

The constant development of new drugs has put on the discussion table the economic impact that these new drugs produce on the different sectors of the health system. Carrying this in what refers to medicines, to the introduction of pharmacoeconomic within the cycle of research and development of a drug. In this way, pharmacoeconomic evaluations have been integrated into the traditional evaluation of efficacy, tolerance, and safety of drugs in the different phases of their clinical development (phase I, II, III and IV), including data necessary for pharmacoeconomic analysis. It is important to note that there are countries, such as Australia, New Zealand, Canada, England and the Netherlands, whose regulatory authorities require cost-effectiveness and cost-utility analysis in decision-making during the process of adopting new treatments. medical notes. Increasingly, pharmaceutical companies need to generate pharmacoeconomic studies adapted to the different markets, to be able to differentiate the advantages for public health that can be derived from the approval, inclusion in formularies and reimbursement systems of their new medicines.

From the above, we can summarize that among the objectives of pharmacoeconomic studies are:

- Specify and measure the different costs involved in the studies pharmacoeconomic.
- Favor the approval of a product.
- Facilitate the inclusion of a product in one or more schemes therapeutic.
- Set the price of a new product.
- Adjust the price of a product already marketed.

Types of Pharmaceconomic Analysis

When reading a pharmacoeconomic study, it is worth paying attention to each of the three aspects that support it: the perspective from which the analysis has been carried out (of the patient, hospital, payer, society, or doctors); the type of costs (direct, indirect, or intangible) and the type of analysis (cost-effectiveness, cost-benefit, cost-minimization, or cost-utility).

The calculation of the costs of health care can be calculated according to different perspectives such as those of the payer (the provision of health in Argentina is covered by three subsectors: public, social security and private), the patient or society (see fig. two). In this sense, it should be noted that the same study carried out from different perspectives can lead to different conclusions:

- That of society, which is the broadest perspective, considering all the costs and consequences. In addition, it prevents the individual interest from being prioritized over that of society.
- That of patients as recipients of the service.
- That of the doctors or providers of the service.
- That of the payers who are the ones who finance the health service.

When evaluating the types of costs in health care, the following four are usually considered-

Direct medical costs are those costs that are associated with the detection, prevention, treatment and/or rehabilitation of a patient. This includes medical fees, fees for laboratory or complementary studies, drug acquisition costs (depending on dose, dosage, and treatment time), observed adverse events and hospitalizations or other interventions. These costs are generally borne either by the state in the case of public care systems, or by social security, or by patients and/or their families.

Direct non-medical costs are those resources consumed by the patient and his family in medical care, affecting the pocket of the patient and his family during the trip to the health center (for example, train, taxi or car). Also included is family time in care provision, which can be work time or free time.

Indirect costs instead represent the cost of morbidity from a disease (time off work) or mortality (premature death) and are calculated by evaluating the loss of productivity in a job due to the individual's illness. In many studies in which indirect costs have been included, they have been even higher than direct medical costs. An example of the importance of indirect costs in economic evaluation is that developed by Blomquist and Ekbom, who analyzed the treatment and direct and indirect costs of inflammatory bowel disease, which includes ulcerative colitis and Crohn's disease, in Sweden during 1994. Direct costs are those related to outpatient care (representing 18% of costs), hospitalization (58%), medication (24% of direct costs and 8% of total costs).

The indirect costs related to the morbidity and mortality of the disease were distributed in: sick leave due to the disease and early retirement. The study's conclusions established that hospitalization costs were mostly concentrated in a few individuals and that morbidity and mortality costs (indirect costs) represented 68% of the total costs.

In a recently published study on cost estimation in cancer patients, it was observed that indirect costs were four times higher for absenteeism and 28 times higher for short-term disability compared to the control group.

Intangible costs include those that entail a loss of well-being for the individual associated with a disease or its treatment (suffering, anxiety, anguish, pain, reduced self-esteem). There is broad agreement about the identification of this type of costs, but not on how to measure and value them due to the difficulty of translating these concepts into economic terms.

An economic evaluation of health costs may include only some or all these types of costs.

In pharmacoeconomic there are 4 types of analysis; all of them measure the costs of health care, but they differ from each other in the measurement and expression of the benefits obtained:

◙ Cost-effectiveness analysis; they compare the costs of an intervention expressed in monetary terms (for example direct and indirect costs) with its effectiveness, measured in clinical terms: number of deaths prevented, disabilities or complications prevented, diseases cured, heart attacks prevented, etc. The results of cost-effectiveness analysis are usually presented as a ratio between costs and clinical effects (e.g., dollars or pesos per life saved, dollars or pesos per 10% mean overall decrease in diastolic pressure).

In this type of analysis, the increases in total costs and clinical effectiveness of a new treatment can be compared with those of conventional treatment.

The results can be obtained from routine clinical practice, or as results of controlled clinical studies.

◙ Cost-benefit analysis: the cost of a medical intervention is compared with the benefit it produces. Both costs and benefits are measured in the same monetary units. Thus, when it is desired to compare the costs and benefits associated with the use of a treatment that could replace another that is already being applied, the increase in the cost of this treatment and the increase in the benefits it produces are valued.

Costs and benefits can be considered positive or negative; in turn a cost can, be incurred or avoided and a benefit can be achieved or lost.

One of the main limitations of the cost-benefit analysis is that the results (benefit provided by the treatment) can be difficult to measure in monetary terms, that is, to express in dollars or pesos a year of life gained, or a disability avoided. In addition, it raises numerous ethical problems derived from assigning monetary values to the results of a treatment.

◙ Cost-utility analysis measures the costs of an intervention expressed in monetary units, and the results in terms of "utility" subjectively assigned by the patient to the overall result of the treatment. A "utility" is a measure of value, according to economists, because of the preferences of patients or society for their state of health. In this sense, individuals can assign a value to different health states and determine the amount of money they would be willing to spend based on clinical improvement. In this way these studies can assess whether individuals want to live longer in poor health or choose a treatment that improves their health but does not prolong their life.

In clinical research, utility values are used to create a criterion or outcome measurement scale from 0 to 100, where 0 represents the worst health state imaginable and 100 the best health state imaginable.

The personal interview using "risk" and "uncertainty" to bring out the preferences of patients is a methodology used. For example, the patient can be asked to choose between a definitive state of health with a certain disability or living the rest of his life in perfect health with the probability of immediate death.

◙ Cost-minimization analysis compares the costs of two or more therapeutic alternatives whose consequences were considered equivalent, choosing the one with the lowest total cost. Before applying this type of analysis, it is necessary to scientifically demonstrate that all the evaluated alternatives produce the same clinical effects or without statistically significant differences (through controlled clinical trials).

The advantage of this type of evaluation is that it allows a complete, simple analysis with great speed in the calculations. The disadvantages are that it does not report on whether the costs exceed the monetary value of the consequences, and it is not possible to make comparisons with other analyses.

From the interpretation of the pharmacoeconomic analyzes comparing the costs and benefits of a new drug (cost-effectiveness, cost-benefit, cost-utility and cost-minimization), they can derive Better, or equal clinical results can be achieved at a lower cost compared to standard treatment, considering this a dominant strategy and one that should be adopted. An increase in costs associated with lower clinical results in relation to conventional treatment is considered a dominated strategy and should always be rejected. The results in the remaining columns are ambiguous and their interpretation will depend on the costs and the clinical results obtained and each one should be analyzed.

More expensive but also more effective therapies should be adopted if the cost-effectiveness ratio falls within an acceptable range and the budget to finance it is also acceptable. Less expensive therapies but with lower results should be analyzed according to the magnitude of the cost and clinical results, without disregarding ethical considerations.

In Oncology, as in other specialties, the search for new therapeutic targets has led to the development of new molecules with sophisticated mechanisms of action and high cost. Representing the access to new medicines an increase in costs of 300% in the last 5 years, triggering more and more that numerous Health Care Systems in the world present severe difficulties to accept high-cost treatments as standard. We know that health resources are limited and waste in one area has repercussions in the lower availability of resources in another, acquiring pharmacoeconomic analysis an important role for adequate decisions in health matters.

The arrival of drugs with new biological targets and high cost, puts more and more on the discussion table how will these costs be faced? and how much is the necessary clinical benefit (impact on survival) that justifies its indiscriminate admission in routine practice? We discuss an example: when the FDA approved first-line treatment for metastatic colorectal cancer, bevacizumab (antiangiogenic agent) in combination with any intravenous chemotherapy based on fluorouracil. This decision generated an intense debate, in relation to the broad spectrum of the combination, indicating that the antiangiogenic effect of bevacizumab is similar when combined with any chemotherapy, while the study that received approval associated it with the combination of irinotecan, fluorouracil and leucovorin (IFL).

Although the study was clinically relevant, demonstrating survival advantages with the association of bevacizumab vs. IFL (20.3 vs. 15.6 respectively), in time to progression (10.6 vs. 6.2 months) and

response rate (44.8% vs. 34.8%), the 4.7-month prolongation in survival was similar to that shown in the study that compared two FOLFOX polychemotherapy regimens (oxaliplatin/fluorouracil/leucovorin) against IFL (19.5 vs. 14.8 months), without disregarding the increased risk of bleeding, hypertension and intestinal perforation in patients receiving antiangiogenic agents.

Numerous questions remain open, however with the arrival of these new drugs with specific biological targets, there is a growing scientific need to compare the clinical benefit of these new high-cost drugs, looking for predictive factors of response that allow us to get closer and closer to individualized therapy.

The rapid proliferation of new drugs has generated that most phase III clinical trials developed by the pharmaceutical industry are part of registration strategies, rather than defining their best use, so we must be cautious with the information available, prevailing the so current "clinical judgment" in the therapeutic indication that balances efficacy, toxicity, and cost.

Conclusions

Recommendations for Approaching A Pharmacoeconomic Study

As with other disciplines, the fashion of pharmacoeconomic has given rise to an exponential increase in the number of publications whose quality has not been uniform. Recent analyzes found that studies funded by pharmaceutical companies were eight times less likely to reach unfavorable qualitative conclusions and 1.4 times more likely to reach favorable conclusions, compared to unfunded studies.

This has led to the formulation of various recommendations on how to approach the conduct of a pharmacoeconomic study:

1- It is essential to previously establish the hypothesis and the objective of the study, considering whether following the scientific method. This means that you have to pose a question that can and will be answered, and that answer is of interest to decision-making at some level.

2- The next step is to determine the perspective of the study, the one that corresponds to the person interested in knowing the results for decision making. For example, a pharmacoeconomic study that justifies the fixing of a price for a new medicine is of fundamental interest to the financier, a study on the saving of hospital resources with the introduction of a new medicine is of interest to the person in charge of the hospital budget.

3- Identify the most relevant costs and consequences, analyzing the data required to value them.

4- Pharmacoeconomic studies do not escape the rules of scientific research methodology and must follow the guidelines of Good Clinical Practices (GCP) in their design and execution.

5- Finally, when presenting the results and conclusions, it is convenient to communicate all the information so that the work is credible, transparent, and reproducible by anyone.

Pharmacoeconomics has made enormous progress in recent years, contributing to raising awareness among physicians, society, and the state about the need to assess health costs. Increasingly, regulatory authorities and those responsible for managing health systems request the results of pharmacoeconomic analyzes to justify the inclusion of a new drug or technology in therapeutic formularies.

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